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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/524,454	03/10/00	BERG	K 697.013US1

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EXAMINER	
EWOLDT,G	
ART UNIT	PAPER NUMBER
1644	9

DATE MAILED: 04/24/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/524,454	Berg et al.
Examiner	**Art Unit**
G. R. Ewoldt	1644

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Feb 16, 2001*.

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-11* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☒ All b) ☐ Some* c) ☐ None of:

1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
18) ☐ Interview Summary (PTO-413) Paper No(s). _____
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. Applicant's election without traverse of Group I, Claims 1-11, in Paper No. 8 is acknowledged.

The requirement is still deemed proper and is therefore made FINAL.

2. Claims 12-21 have been canceled, therefore, all pending claims are drawn to the elected invention and are being acted upon.

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 C.F.R. 1.821 through 1.825 for the reason(s) set forth on the attached Notice To Comply With Requirements For Patent Applications Containing Nucleotide Sequence And/Or Amino Acid Sequence Disclosures. Specifically, the sequence on page 21, line 17, of the specification must comply with sequence requirements.

4. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

5. Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification does not reasonably provide enablement for: a method of expressing an antigenic molecule or a part thereof on the surface of a cell comprising photochemical internalization (PDI),

A) wherein the antigenic molecule is a molecule capable of stimulating an immune response,

B) wherein the antigenic presentation results in the stimulation of an immune response,

C) wherein the antigenic molecule is a vaccine antigen or vaccine component (Claim 3).

Note that while the limitations of A and B, are recited in Claims 3 and 11 respectively, said limitations must also apply to independent Claim 1 as well, given the intended use of the claimed invention. Antigen (or "antigenic molecule" as recited in Claim 1) is defined as "a substance that can induce a detectable immune response" (Stites et al., 1987). Further, page 4 of the specification discloses that cell surface expression of molecules has utility "in the field of vaccination" "in order to induce, facilitate, or augment an immune response." Thus, the limitations of Claims 3 and 11 also apply to Claim 1.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without an undue amount of experimentation. The scope of the claims are not commensurate with the enablement provided by the disclosure with regard to the breadth of the claims.

Regarding a method of expressing an antigenic molecule or a part thereof on the surface of a cell comprising photochemical internalization resulting in the stimulation of an immune response, Lynch et al. (1989) teaches that PDI, also known as photodynamic therapy (PDT), is actually immunosuppressive, and that said immunosuppression is actually adoptively transferable through macrophages (see particularly RESULTS). Further, U.S. Patent No. 6,153,639 teaches that PDT can downregulate MHC Class I molecules (see particularly column 12, lines 15-30). Said downregulation would be expected to result in immunosuppression. Given these prior art teachings, significant working examples would be required to enable claims drawn to the opposite effect, i.e., immunostimulation or immune induction.

Of the four examples disclosed in the specification, none offer substantial support for the claimed invention. Example 1 merely discloses photochemicals and peptides can be internalized. Example 2 discloses a cytotoxic assay in which PDT is asserted to induce the internalization of a peptide followed by induction of an *in vitro* CTL response to said peptide. However, as the example does not disclose appropriate controls, i.e., a cytotoxic assay absent the photosensitizing agent and a cytotoxic assay absent photostimulation, the results of the example can not be interpreted. Example 4 is irrelevant to the claimed invention as it discloses the delivery of DNA to a cell, and Example 3 actually appears to teach away from the claimed invention. The results of Example 3, as disclosed in Figure 4, show that PDT merely induces internalization of a molecule (as found in the cytosol, filled circles) and not cell surface expression (as found on the cell corpses, filled triangles). Thus the use of

the invention as claimed would be highly unpredictable and requiring of significantly more enablement, i.e., working examples, than is disclosed in the specification.

Regarding a vaccine antigen or component, a vaccine is defined as a composition for the prevention of infectious diseases (Stites et al., 1987). The instant specification offers no support for a claim to the prevention of any disease, and indeed a claim to such would require significantly more enablement than claims to mere immunostimulation which itself is insufficiently supported.

It is also noted that the prior art teaches that PDT is potently cytotoxic. See for example, Lapes et al. (1996) in which one of the claimed photosensitizing agents ($TPPS_4$) is taught to be highly cytotoxic (see particularly RESULTS). Thus the use of the invention as claimed would again be highly unpredictable and requiring of significantly more enablement, i.e., working examples, than is disclosed in the specification.

In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. Thus, in view of the quantity of experimentation necessary, the lack of any working examples, the unpredictability of the art, and the lack of sufficient guidance in the specification regarding both how to make the claimed invention, it would take undue trials and errors to practice the invention of the instant claims.

6. Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

There is insufficient written description to show that Applicant was in possession of the claimed "part thereof" of an antigenic molecule. Absent any specific definition for "part thereof" of an antigenic molecule, said "part thereof" would encompass even single amino acids. Likewise, the recitation of "derivatives thereof" of photosensitizing agents (Claim 7), absent any particular limitation, would encompass an unlimited number of compounds and compositions, none of which are disclosed by the specification. One of skill in the art would therefore conclude that the specification fails to disclose a

representative number of species to describe the claimed genuses. See *Eli Lilly*, 119 F.3d 1559, 43 USPQ2d 1398.

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

8. Claims 6-8 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

A) the plurals lymphocytes, dendritic cells, macrophages and cancer cells have no antecedent basis in the singular "cell" in the preamble of Claim 6,

B) the plural photosensitizing agents have no antecedent basis in the singular "photosensitizing agent" in the preamble of Claim 7,

C) the abbreviations "$TPPS_4$, $TPPS_{2a}$, and $AlPcS_{2a}$" render the claim indefinite because they have not been defined in claim 8.

9. No claim is allowed.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (703) 308-9805. The examiner can normally be reached Monday through Thursday and alternate Fridays from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

G.R. Ewoldt, Ph.D.
Patent Examiner
Technology Center 1600
April 18, 2001

Patrick J. Nolan, Ph.D.
Primary Examiner
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